

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 3 of 89

II. AMENDMENT TO THE CLAIMS

▪ Format of Claim Amendments

Applicant has amended the claims as indicated below. Pursuant to the revised format to 37 C.F.R. 1.121 which is planned to be officially adopted by the USPTO in July of 2003, and which is now permitted by the office pursuant to the USPTO's release of January 31, 2003, Applicants herein submit only one version of the claims with markings to show changes. A detailed listing of all claims that are, or were in the application, are presented.

▪ Statement with Respect to Scope of Amended and Non-Amended Claims

Amendments to, cancellation of, and additions to, the claims are made in order to streamline prosecution of the case to embodiments that are presently anticipated to be of commercial significance, and are not made for a purpose of patentability. Any amendment, cancellation or addition made herein should not be construed in any manner as indicating Applicants' surrender of any subject matter of the application, or surrender of any equivalent to any element asserted in one or more claims. Applicants do not concede that the scope of the claims set forth below fail to extend as far as the original claims. Furthermore, any narrowing which may be evinced with respect to subject matter covered by the claims as a whole, or by one or more claims of the appended claims, when compared to claims previously in the application, should not be interpreted as indicating that the Applicants have generally disclaimed the territory between the original claimed subject matter and the amended claimed subject matter. Applicants intend each term of the claims set forth below to be read with respect to the full-breadth of the language of the claims and not to be confined to a strict literal read of amended terms. Amended claims elements are to be construed to include substantial equivalents known to those of ordinary skill in the art. Applicants assert that the amendments are made without prejudice and reserve all rights to prosecute any canceled claims, and claims preceding any amendment, and other disclosed (but not presently claimed) embodiments in the application, in future continuation applications, divisional applications, continuation-in-part applications, continuing prosecution applications, requests for continuing examination, re-examination applications and any other application claiming priority from or through the present application.

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 4 of 89

**COMPLETE LIST OF CLAIMS THAT ARE OR HAVE BEEN BEFORE THE
OFFICE AFTER ENTRANCE OF THE AMENDMENTS MADE HEREIN**

(See next page)

CT01/HOFFHA/216624.1

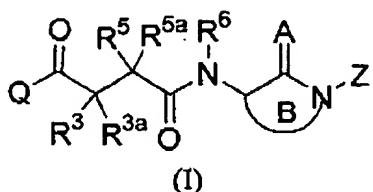
PAGE 5/90 * RCVD AT 7/8/2005 12:54:20 PM [Eastern Daylight Time] * SVR:USPTO-EXRF-1/3 * DNI:8729306 * CSID:203 351 8128 * DURATION (mm:ss):21:12

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 5 of 89

1.

(CURRENTLY AMENDED) A compound of Formula (I):



or a pharmaceutically acceptable salt thereof, wherein:

A is O or S;

Q is -NR¹R²;R¹ is selected from: H and C₁-C₆ alkyl;R² is independently selected from H and C₁-C₆ alkyl;R³ is -(CR⁷R^{7a})_n-R⁴,

- (CR⁷R^{7a})_n-S-(CR⁷R^{7a})_m-R⁴,
- (CR⁷R^{7a})_n-O-(CR⁷R^{7a})_m-R⁴,
- (CR⁷R^{7a})_n-N(R^{7b})-(CR⁷R^{7a})_m-R⁴,
- (CR⁷R^{7a})_n-S(=O)-(CR⁷R^{7a})_m-R⁴,
- (CR⁷R^{7a})_n-S(=O)2-(CR⁷R^{7a})_m-R⁴,
- (CR⁷R^{7a})_n-C(=O)-(CR⁷R^{7a})_m-R⁴,
- (CR⁷R^{7a})_n-N(R^{7b})C(=O)-(CR⁷R^{7a})_m-R⁴,
- (CR⁷R^{7a})_n-C(=O)N(R^{7b})-(CR⁷R^{7a})_m-R⁴,
- (CR⁷R^{7a})_n-N(R^{7b})S(=O)2-(CR⁷R^{7a})_m-R⁴, or
- (CR⁷R^{7a})_n-S(=O)2N(R^{7b})-(CR⁷R^{7a})_m-R⁴;

n is 0, 1, 2, or 3;

m is 0, 1, 2, or 3;

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 6 of 89

R^3a is H, OH, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₂-C₄ alkenyl
or C₂-C₄ alkenyloxy;

R^4 is H, OH, OR^{14a},
C₁-C₆ alkyl substituted with 0-3 R^{4a},
C₂-C₆ alkenyl substituted with 0-3 R^{4a},
C₂-C₆ alkynyl substituted with 0-3 R^{4a},
C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,
C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,
NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl,
C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

R^5 is H, OR¹⁴;
C₁-C₆ alkyl substituted with 0-3 R^{5b};
C₁-C₆ alkoxy substituted with 0-3 R^{5b};
C₂-C₆ alkenyl substituted with 0-3 R^{5b};
C₂-C₆ alkynyl substituted with 0-3 R^{5b};
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 7 of 89

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5a} is H, OH, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₂-C₄ alkenyl, or C₂-C₄ alkenyloxy;

R^{5b}, at each occurrence, is independently selected from:

H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶;
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

R⁶ is H;

C₁-C₆ alkyl substituted with 0-3 R^{6a};
C₃-C₁₀ carbocycle substituted with 0-3 R^{6b}; or
C₆-C₁₀ aryl substituted with 0-3 R^{6b};

R^{6a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, aryl or CF₃;

R^{6b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁷, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl and C₁-C₄ alkyl;

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 8 of 89*

R^{7a} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;

R^{7b} is independently selected from H and C₁-C₄ alkyl;

Ring B is a 7 membered lactam or thiolactam,

wherein the lactam is 2-oxo-azepinyl or thiolactam is 2-thioxo-azepinyl;

wherein each additional lactam carbon or thiolactam carbon is substituted with 0-2 R^{11} ;
provided two R^{11} substituents are present on adjacent atoms and are combined to
form a benzo fused radical; wherein said benzo fused radical is substituted with 0-4
 R^{13} ;

and,

wherein the lactam or thiolactam contains a heteroatom selected from -N=, -NH-, and -
 $N(R^{10})$ -;

R^{10} is H, C(=O) R^{17} , C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹,
S(=O)₂NR¹⁸R¹⁹, S(=O)₂R¹⁷;

C₁-C₆ alkyl optionally substituted with 0-3 R^{10a} ;

C₆-C₁₀ aryl substituted with 0-4 R^{10b} ;

C₃-C₁₀ carbocycle substituted with 0-3 R^{10b} ; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{10b} ;

R^{10a} , at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O,
CN, NO₂, NR¹⁵R¹⁶, CF₃, or aryl substituted with 0-4 R^{10b} ;

R^{10b} , at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy,
Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆
alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

R^{11} , at each occurrence, is independently selected from

CT01/HOFFHΛ/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
 Mailed 04/08/2005
 Page 9 of 89

H, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷,
 C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, CF₃;
 C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};
 C₆-C₁₀ aryl substituted with 0-3 R^{11b};
 C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from
 H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃;
 phenyl substituted with 0-3 R^{11b};
 C₃-C₆ cycloalkyl substituted with 0-3 R^{11b}; and
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

Z is H;

C₁-C₈ alkyl substituted with 1-3 R¹²;
 C₂-C₄ alkenyl substituted with 1-3 R¹²;
 C₂-C₄ alkynyl substituted with 1-3 R¹²;
 C₁-C₈ alkyl substituted with 0-3 R^{12a};
 C₂-C₄ alkenyl substituted with 0-3 R^{12a};
 C₂-C₄ alkynyl substituted with 0-3 R^{12a};
 C₆-C₁₀ aryl substituted with 0-4 R^{12b};
 C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

CT01/HOFFH/V216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 10 of 89*

R^{12} , at each occurrence, is independently selected from

C_6-C_{10} aryl substituted with 0-4 R^{12b} ;
 C_3-C_{10} carbocycle substituted with 0-4 R^{12b} ; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b} ;

R^{12a} , at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, -C(=O)NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, or C₁-C₄ haloalkyl-S-;

R^{12b} , at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

R^{13} , at each occurrence, is independently selected from

H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R^{14} is H, phenyl, benzyl, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl, or C₃-C₆ cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C₁-C₄ alkyl;

R^{15} , at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R^{16} , at each occurrence, is independently selected from

H, OH, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R^{17} is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 11 of 89*

aryl substituted by 0-4 R^{17a}, or
 $-\text{CH}_2\text{-aryl}$ substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

R^{18} , at each occurrence, is independently selected from H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-; and

R¹⁹, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

provided, when R^{13} is H,

then Z is H :

C₄-C₈ alkyl substituted with 1-3 R¹²:

C₂-C₄ alkenyl substituted with 1-3 R¹²:

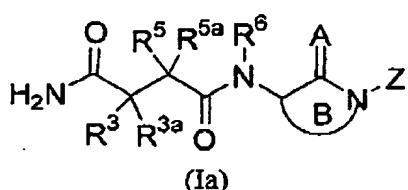
C₂-C₄ alkynyl substituted with 1-3 R¹²:

C₁-C₈ alkyl substituted with 0-3 R^{12a}.

C2-C4 alkenyl substituted with 0-3 R^{12a}, or

C2-C4 alkynyl substituted with 0-3 R^{12a}

2. (PREVIOUSLY PRESENTED) A compound, according to Claim 1, of Formula (Ia):



or a pharmaceutically acceptable salt thereof,
wherein:

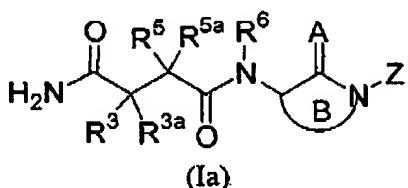
U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 12 of 89

Z is H;

C₁-C₈ alkyl substituted with 0-3 R^{12a};C₂-C₄ alkenyl substituted with 0-3 R^{12a}; orC₂-C₄ alkynyl substituted with 0-3 R^{12a}.

3. (CURRENTLY AMENDED) A compound according to Claim 2 of Formula (Ia)



or a pharmaceutically acceptable salt thereof,

wherein:

R³ is -(CR⁷R^{7a})_n-R⁴,-(CR⁷R^{7a})_n-S-(CR⁷R^{7a})_m-R⁴,-(CR⁷R^{7a})_n-O-(CR⁷R^{7a})_m-R⁴, or-(CR⁷R^{7a})_n-N(R^{7b})-(CR⁷R^{7a})_m-R⁴;

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;R⁴ is H, OH, OR^{14a},C₁-C₆ alkyl substituted with 0-3 R^{4a},C₂-C₆ alkenyl substituted with 0-3 R^{4a},C₂-C₆ alkynyl substituted with 0-3 R^{4a},C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 13 of 89

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃, C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁵ is H, OR¹⁴;
C₁-C₆ alkyl substituted with 0-3 R^{5b};
C₁-C₆ alkoxy substituted with 0-3 R^{5b};
C₂-C₆ alkenyl substituted with 0-3 R^{5b};
C₂-C₆ alkynyl substituted with 0-3 R^{5b};
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5a} is H or C₁-C₄ alkyl;

R^{5b}, at each occurrence, is independently selected from:
H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶,
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
 Mailed 04/08/2005
 Page 14 of 89

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

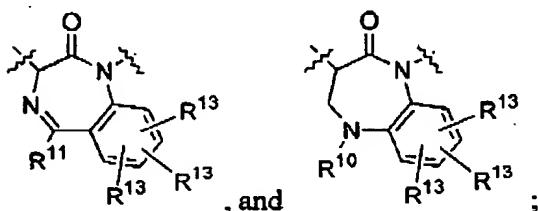
R⁶ is H, methyl, or ethyl;

R⁷, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl and C₁-C₄ alkyl;

R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is selected from



R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹,

S(=O)₂NR¹⁸R¹⁹, S(=O)₂R¹⁷;

C₁-C₆ alkyl optionally substituted with 0-2 R^{10a};

C₆-C₁₀ aryl substituted with 0-4 R^{10b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{10b}; or

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 15 of 89

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, or CF₃;

R¹¹, at each occurrence, is independently selected from
H, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷,
C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, CF₃;
C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};
C₆-C₁₀ aryl substituted with 0-3 R^{11b};
C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

Z is H;

C₁-C₆ alkyl substituted with 0-3 R^{12a};
C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or
C₂-C₄ alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from

CT01/HOFFMAN/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 16 of 89

H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)2CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R¹³, at each occurrence, is independently selected from

H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)2-;

R¹⁶, at each occurrence, is independently selected from

H, OH, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)2-;

R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,

aryl substituted by 0-4 R^{17a}, or
 -CH₂-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

R¹⁸, at each occurrence, is independently selected from

H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)2-; and

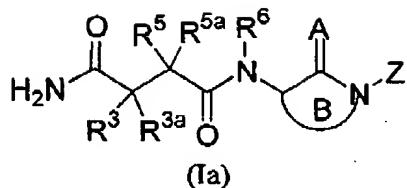
R¹⁹, at each occurrence, is independently selected from

H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)2-.

4. (CURRENTLY AMENDED) A compound according to Claim 3 of Formula (Ia)

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 17 of 89

or a pharmaceutically acceptable salt thereof,

wherein:

R³ is -(CHR⁷)_n-R⁴,

n is 0 or 1;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;R⁴ is H, OH, OR^{14a},C₁-C₄ alkyl substituted with 0-2 R^{4a},C₂-C₄ alkenyl substituted with 0-2 R^{4a},C₂-C₄ alkynyl substituted with 0-1 R^{4a},C₃-C₆ carbocycle substituted with 0-3 R^{4b},C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,

oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,C₃-C₆ carbocycle substituted with 0-3 R^{4b},phenyl substituted with 0-3 R^{4b}, or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,

oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
 Mailed 04/08/2005
 Page 18 of 89

R^{4b} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2 , $NR^{15}R^{16}$, CF_3 , acetyl, SCH_3 , $S(=O)CH_3$, $S(=O)_2CH_3$, C_1 - C_4 alkyl, C_1 - C_3 alkoxy, C_1 - C_2 haloalkyl, and C_1 - C_2 haloalkoxy;

R^5 is H, OR^{14} ;
 C_1 - C_4 alkyl substituted with 0-3 R^{5b} ;
 C_2 - C_4 alkenyl substituted with 0-3 R^{5b} ;
 C_2 - C_4 alkynyl substituted with 0-3 R^{5b} ;

R^{5a} is H, methyl, ethyl, propyl, or butyl;

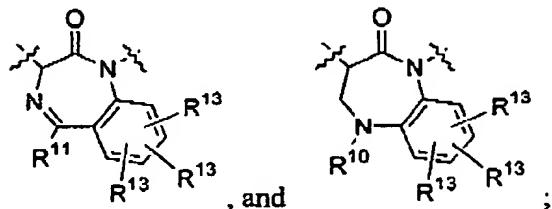
R^{5b} , at each occurrence, is independently selected from:
 H, methyl, ethyl, propyl, butyl, CF_3 , OR^{14} , Cl, F, Br, I, =O;
 C_3 - C_6 carbocycle substituted with 0-3 R^{5c} ;
 phenyl substituted with 0-3 R^{5c} ; or
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c} ;

R^{5c} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2 , $NR^{15}R^{16}$, CF_3 , acetyl, SCH_3 , $S(=O)CH_3$, $S(=O)_2CH_3$, C_1 - C_4 alkyl, C_1 - C_3 alkoxy, C_1 - C_2 haloalkyl, and C_1 - C_2 haloalkoxy;

R^6 is H;

R^7 , at each occurrence, is independently selected from H, F, CF_3 , methyl, and ethyl;

Ring B is selected from



CT01/HOFFHA/216524.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 19 of 89

R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$;
 C_1 - C_4 alkyl optionally substituted with 0-1 R^{10a} ;
phenyl substituted with 0-4 R^{10b} ;
 C_3 - C_6 carbocycle substituted with 0-3 R^{10b} ; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{10b} ;

R^{10a} is selected from H, C_1 - C_4 alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b} ;

R^{10b} , at each occurrence, is independently selected from H, OH, C_1 - C_4 alkyl, C_1 - C_3 alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, or CF₃;

R^{11} is selected from
H, C_1 - C_4 alkoxy, Cl, F, NR¹⁸R¹⁹, $C(=O)R^{17}$, $C(=O)OR^{17}$, CF₃;
 C_1 - C_6 alkyl optionally substituted with 0-3 R^{11a} ;
 C_6 - C_{10} aryl substituted with 0-3 R^{11b} ;
 C_3 - C_6 carbocycle substituted with 0-3 R^{11b} ; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b} ;

R^{11a} , at each occurrence, is independently selected from H, C_1 - C_4 alkyl, OR¹⁴, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b} ;

R^{11b} , at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, C_1 - C_4 alkyl, C_1 - C_3 alkoxy, C_1 - C_2 haloalkyl, and C_1 - C_2 haloalkoxy;

Z is H;
 C_1 - C_4 alkyl substituted with 0-3 R^{12a} ;
 C_2 - C_4 alkenyl substituted with 0-3 R^{12a} ; or

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 20 of 89*

C₂-C₄ alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from

*H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl,
C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;*

R¹³, at each occurrence, is independently selected from

H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₄ alkyl, or C₂-C₄ alkoxyalkyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)2-;

R¹⁶, at each occurrence, is independently selected from

*H, OH, C₁-C₄ alkyl, benzyl, phenethyl,
(C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)2-;*

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl,

ethoxyethyl,

phenyl substituted by 0-3 R^{17a}, or

-CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

R¹⁸, at each occurrence, is independently selected from

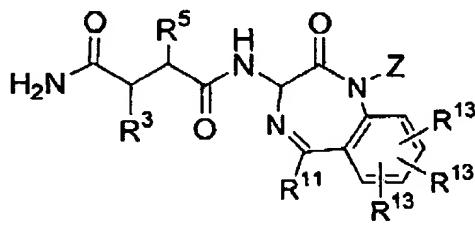
H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from

H, methyl, and ethyl.

5. (Canceled)

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 21 of 896. (CURRENTLY AMENDED) A compound according to Claim 4 of Formula (Ic)

(Ic)

or a pharmaceutically acceptable salt thereof
wherein

R³ is R⁴,

R⁴ is C₁-C₄ alkyl substituted with 0-1 R^{4a},
C₂-C₄ alkenyl substituted with 0-1 R^{4a}, or
C₂-C₄ alkynyl substituted with 0-1 R^{4a};

R^{4a} is selected from:
H, F, CF₃,
C₃-C₆ carbocycle substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 22 of 89

R^5 is C₁-C₄ alkyl substituted with 0-1 R^{5b} ;
 C₂-C₄ alkenyl substituted with 0-1 R^{5b} ;
 C₂-C₄ alkynyl substituted with 0-1 R^{5b} ;

R^{5b} is selected from:

H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, =O;
 C₃-C₆ carbocycle substituted with 0-2 R^{5c} ;
 phenyl substituted with 0-3 R^{5c} ; or
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c} ; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thieryl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c} , at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R^{11} is selected from

H, NR¹⁸R¹⁹, CF₃;
 C₁-C₄ alkyl optionally substituted with 0-1 R^{11a} ;
 phenyl substituted with 0-3 R^{11b} ;
 C₃-C₆ carbocycle substituted with 0-3 R^{11b} ; and
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b} ; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thieryl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a} is selected from H, C₁-C₄ alkyl, OR¹⁴, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b} ;

R^{11b} , at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 23 of 89

Z is H;

C₁-C₄ alkyl substituted with 0-3 R^{12a};C₂-C₄ alkenyl substituted with 0-3 R^{12a}; orC₂-C₄ alkynyl substituted with 0-3 R^{12a};R^{12a}, at each occurrence, is independently selected fromH, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;R¹³, at each occurrence, is independently selected fromH, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;R¹⁵, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;R¹⁶, at each occurrence, is independently selected fromH, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-S(=O)₂-, and ethyl-S(=O)₂-;R¹⁸, at each occurrence, is independently selected from

H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from

H, methyl, and ethyl.

7. - 9 (CANCELLED)**10. (PREVIOUSLY PRESENTED)** A compound, according to Claim 6, wherein:

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 24 of 89

R³ is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH₂CH₂CH₂CH₃,
-CH(CH₃)₂, -CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂,
-CH₂CF₃, -CH₂CH₂CF₃, -CH₂CH₂CH₂CF₃,
-CH=CH₂, -CH₂CH=CH₂, -CH₂C(CH₃)=CH₂,
-CH₂CH₂CH=CH₂,
cis-CH₂CH=CH(CH₃),
trans-CH₂CH=CH(CH₃),
-C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃),
cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-, cyclohexyl-CH₂-, cyclopropyl-CH₂CH₂-,
cyclobutyl-CH₂CH₂-, cyclopentyl-CH₂CH₂-,
cyclohexyl-CH₂CH₂-, phenyl-CH₂-,
(2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-, (4-F-phenyl)CH₂-,
(2-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂-,
(2,3-diF-phenyl)CH₂-, (2,4-diF-phenyl)CH₂-,
(2,5-diF-phenyl)CH₂-, (2,6-diF-phenyl)CH₂-,
(3,4-diF-phenyl)CH₂-, (3,5-diF-phenyl)CH₂-,
(2,3-diCl-phenyl)CH₂-, (2,4-diCl-phenyl)CH₂-,
(2,5-diCl-phenyl)CH₂-, (2,6-diCl-phenyl)CH₂-,
(3,4-diCl-phenyl)CH₂-, (3,5-diCl-phenyl)CH₂-,
(3-F-4-Cl-phenyl)CH₂-, (3-F-5-Cl-phenyl)CH₂-,
(3-Cl-4-F-phenyl)CH₂-, phenyl-CH₂CH₂-,
(2-F-phenyl)CH₂CH₂-, (3-F-phenyl)CH₂CH₂-,
(4-F-phenyl)CH₂CH₂-, (2-Cl-phenyl)CH₂CH₂-,
(3-Cl-phenyl)CH₂CH₂-, (4-Cl-phenyl)CH₂CH₂-,
(2,3-diF-phenyl)CH₂CH₂-, (2,4-diF-phenyl)CH₂CH₂-,
(2,5-diF-phenyl)CH₂CH₂-, (2,6-diF-phenyl)CH₂CH₂-,
(3,4-diF-phenyl)CH₂CH₂-, (3,5-diF-phenyl)CH₂CH₂-,
(2,3-diCl-phenyl)CH₂CH₂-, (2,4-diCl-phenyl)CH₂CH₂-,
(2,5-diCl-phenyl)CH₂CH₂-, (2,6-diCl-phenyl)CH₂CH₂-,
(3,4-diCl-phenyl)CH₂CH₂-, (3,5-diCl-phenyl)CH₂CH₂-,
(3-F-4-Cl-phenyl)CH₂CH₂-, or (3-F-5-Cl-phenyl)CH₂CH₂-,

R⁵ is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH(CH₃)₂, -CH₂CH₂CH₂CH₃,

CT01/HOFFMAN/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
 Mailed 04/08/2005
 Page 25 of 89

-CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂, -CH₂C(CH₃)₃,
 -CH₂CH₂CH₂CH₂CH₃, -CH(CH₃)CH₂CH₂CH₃, -CH₂CH(CH₃)CH₂CH₃,
 -CH₂CH₂CH(CH₃)₂, -CH(CH₂CH₃)₂, -CH₂CF₃, -CH₂CH₂CF₃,
 -CH₂CH₂CH₂CF₃, -CH₂CH₂CH₂CH₂CF₃, -CH=CH₂, -CH₂CH=CH₂,
 -CH=CHCH₃, cis-CH₂CH=CH(CH₃), trans-CH₂CH=CH(CH₃),
 trans-CH₂CH=CH(C₆H₅), -CH₂CH=C(CH₃)₂, cis-CH₂CH=CHCH₂CH₃,
 trans-CH₂CH=CHCH₂CH₃, cis-CH₂CH₂CH=CH(CH₃),
 trans-CH₂CH₂CH=CH(CH₃), trans-CH₂CH=CHCH₂(C₆H₅),
 -C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃), -CH₂C≡C(C₆H₅),
 -CH₂CH₂C≡CH, -CH₂CH₂C≡C(CH₃), -CH₂CH₂C≡C(C₆H₅),
 cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-,
 cyclohexyl-CH₂-, (2-CH₃-cyclopropyl)CH₂-,
 (3-CH₃-cyclobutyl)CH₂-,
 cyclopropyl-CH₂CH₂-, cyclobutyl-CH₂CH₂-,
 cyclopentyl-CH₂CH₂-, cyclohexyl-CH₂CH₂-,
 (2-CH₃-cyclopropyl)CH₂CH₂-, (3-CH₃-cyclobutyl)CH₂CH₂-,
 phenyl-CH₂-, (2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-,
 (4-F-phenyl)CH₂-, furanyl-CH₂-, thienyl-CH₂-,
 pyridyl-CH₂-, 1-imidazolyl-CH₂-, oxazolyl-CH₂-,
 isoxazolyl-CH₂-,
 phenyl-CH₂CH₂-, (2-F-phenyl)CH₂CH₂-, (3-F-phenyl)CH₂CH₂-,
 (4-F-phenyl)CH₂CH₂-, furanyl-CH₂CH₂-, thienyl-CH₂CH₂-,
 pyridyl-CH₂CH₂-, 1-imidazolyl-CH₂CH₂-, oxazolyl-CH₂CH₂-,
 isoxazolyl-CH₂CH₂;

Z is methyl, ethyl, i-propyl, n-propyl, n-butyl, i-butyl, s-butyl, t-butyl, or allyl;

R¹¹, at each occurrence, is independently selected from

H, methyl, ethyl, phenyl, benzyl, phenethyl,
 4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,
 3-F-phenyl, (3-F-phenyl)CH₂-, (3-F-phenyl)CH₂CH₂-,
 2-F-phenyl, (2-F-phenyl)CH₂-, (2-F-phenyl)CH₂CH₂-,
 4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,
 3-Cl-phenyl, (3-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂CH₂-,

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 26 of 89

4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,
3-CH₃-phenyl, (3-CH₃-phenyl)CH₂-, (3-CH₃-phenyl)CH₂CH₂-,
4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, (4-CF₃-phenyl)CH₂CH₂-,
pyrid-2-yl, pyrid-3-yl, or pyrid-4-yl, and

R¹³, at each occurrence, is independently selected from
H, F, Cl, OH, -CH₃, -CH₂CH₃, -OCH₃, or -CF₃.

11. (PREVIOUSLY AMENDED) A compound according to Claim 2 selected from:

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-methyl-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-methyl-3-allyl-butanediamide;

*U.S. Appl. No. 09/505,788; filed Feb 17, 2005**Response to Final Office Action
Mailed 04/08/2005
Page 27 of 89*

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-methyl-3-propyl-butanediamide;

(2R) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-methyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(2-fluorophenyl)-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(2-fluorophenyl)-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(2-fluorophenyl)-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2S,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 28 of 89*

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(2-fluorophenyl)-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[(1,3-dihydro-1-methyl-2-oxo-5-(4-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(4-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(1,3-dihydro-1-methyl-2-oxo-5-(pyrid-2-yl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(1,3-dihydro-1-methyl-2-oxo-5-(N-morpholino)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(1,3-dihydro-1-methyl-2-oxo-5-(dimethylamino)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(1,3-dihydro-1-methyl-2-oxo-5-(N-methyl-N-phenylamino)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(1,3-dihydro-1-methyl-2-oxo-5-(N-piperidinyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(1,3-dihydro-1-methyl-2-oxo-5-(N-homopiperidinyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(1,3-dihydro-1-methyl-2-oxo-5-(3-methoxyphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 29 of 89*

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(pyrid-4-yl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-methoxy-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(pyrid-3-yl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(cyclopropylmethyl)-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(3-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(3-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(3-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(3-buten-1-yl)-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(cyclopentylethyl)-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(3-buten-1-yl)-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(3-buten-1-yl)-butanediamide;

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action

Mailed 04/08/2005

Page 30 of 89

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-n-butyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-chlorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(3-buten-1-yl)-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-chlorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-n-butyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-N4-[benzyl]-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-methyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-n-butyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(2-methylpropyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action

Mailed 04/08/2005

Page 31 of 89

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(4-chlorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

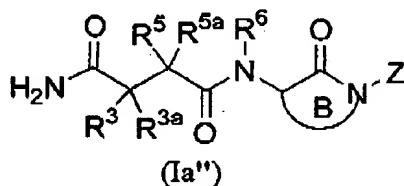
(2R,3S) N1-[1,3-dihydro-1-ethyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-propyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-(isopropyl)-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide; and

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3,3-diallyl-butanediamide.

12. (CURRENTLY AMENDED) A compound, according to Claim 1, of Formula (Ia''):



or a pharmaceutically acceptable salt thereof,

wherein:

Z is C₁-C₈ alkyl substituted with 1-3 R¹²;

C₂-C₄ alkenyl substituted with 1-3 R¹²;

C₂-C₄ alkynyl substituted with 1-3 R¹²;

C₆-C₁₀ aryl substituted with 0-4 R^{12b};

C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or

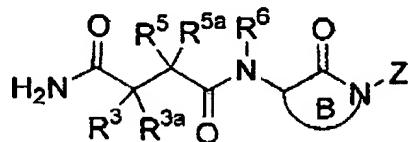
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 32 of 89

provided, when R¹³ is H,
 then Z is C₄-C₈ alkyl substituted with 1-3 R¹²;
 C₂-C₄ alkenyl substituted with 1-3 R¹²; or
 C₂-C₄ alkynyl substituted with 1-3 R¹².

13. (CURRENTLY AMENDED) A compound according to Claim 12 of Formula (Ia'')



(Ia'')

or a pharmaceutically acceptable salt thereof,
 wherein:

R³ is -(CR⁷R^{7a})_n-R⁴,
 -(CR⁷R^{7a})_n-S-(CR⁷R^{7a})_m-R⁴,
 -(CR⁷R^{7a})_n-O-(CR⁷R^{7a})_m-R⁴, or
 -(CR⁷R^{7a})_n-N(R^{7b})-(CR⁷R^{7a})_m-R⁴;

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},
 C₁-C₆ alkyl substituted with 0-3 R^{4a},
 C₂-C₆ alkenyl substituted with 0-3 R^{4a},
 C₂-C₆ alkynyl substituted with 0-3 R^{4a},

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 33 of 89C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy,C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;R⁵ is H, OR¹⁴;C₁-C₆ alkyl substituted with 0-3 R^{5b};C₁-C₆ alkoxy substituted with 0-3 R^{5b};C₂-C₆ alkenyl substituted with 0-3 R^{5b};C₂-C₆ alkynyl substituted with 0-3 R^{5b};C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};R^{5a} is H or C₁-C₄ alkyl;R^{5b}, at each occurrence, is independently selected from:H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶;C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

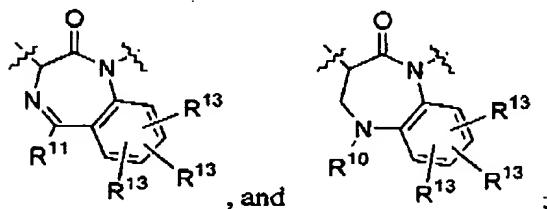
Response to Final Office Action

Mailed 04/08/2005

Page 34 of 89

 $\text{C}_6\text{-C}_{10}$ aryl substituted with 0-3 R^{5c} ; or5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c} ; R^{5c} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy; R^6 is H, methyl, or ethyl; R^7 , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl, and C₁-C₄ alkyl; R^{7a} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl; R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is selected from



R^{10} is H, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, S(=O)₂R¹⁷; C₁-C₆ alkyl optionally substituted with 0-2 R^{10a} ; $\text{C}_6\text{-C}_{10}$ aryl substituted with 0-4 R^{10b} ; C₃-C₁₀ carbocycle substituted with 0-3 R^{10b} ; or

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action

Mailed 04/08/2005

Page 35 of 89

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, or CF₃;

R¹¹, at each occurrence, is independently selected from
H, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷,
C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, CF₃;
C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};
C₆-C₁₀ aryl substituted with 0-3 R^{11b};
C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

Z is C₁-C₆ alkyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²;
C₂-C₄ alkynyl substituted with 1-3 R¹²;
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action

Mailed 04/08/2005

Page 36 of 89

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R¹², at each occurrence, is independently selected from

C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R¹³, at each occurrence, is independently selected from

H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from

H, OH, C₁-C₆ alkyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,

aryl substituted by 0-4 R^{17a}, or
-CH₂-aryl substituted by 0-4 R^{17a};

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action

Mailed 04/08/2005

Page 37 of 89

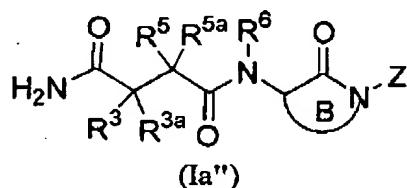
R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

R¹⁸, at each occurrence, is independently selected from
H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-; and

R¹⁹, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

provided, when R¹³ is H,
then Z is C₄-C₆ alkyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²; or
C₂-C₄ alkynyl substituted with 1-3 R¹².

14. (CURRENTLY AMENDED) A compound according to Claim 13 of Formula (Ia'')



or a pharmaceutically acceptable salt thereof,
wherein:

R³ is -(CHR⁷)_n-R⁴,

n is 0 or 1;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action

Mailed 04/08/2005

Page 38 of 89

C₁-C₄ alkyl substituted with 0-2 R^{4a},
 C₂-C₄ alkenyl substituted with 0-2 R^{4a},
 C₂-C₄ alkynyl substituted with 0-1 R^{4a},
 C₃-C₆ carbocycle substituted with 0-3 R^{4b},
 C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃, C₃-C₆ carbocycle substituted with 0-3 R^{4b}, phenyl substituted with 0-3 R^{4b}, or 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is H, OR¹⁴,
 C₁-C₄ alkyl substituted with 0-3 R^{5b},
 C₂-C₄ alkenyl substituted with 0-3 R^{5b},
 C₂-C₄ alkynyl substituted with 0-3 R^{5b};

R^{5a} is H, methyl, ethyl, propyl, or butyl;

R^{5b}, at each occurrence, is independently selected from:
 H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, Cl, F, Br, I, =O;
 C₃-C₆ carbocycle substituted with 0-3 R^{5c}, phenyl substituted with 0-3 R^{5c}; or
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c};

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action

Mailed 04/08/2005

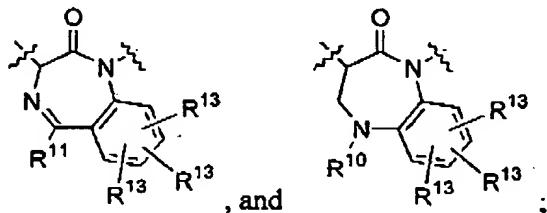
Page 39 of 89

R^{5c} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R^6 is H;

R^7 , at each occurrence, is independently selected from H, F, CF₃, methyl, and ethyl;

Ring B is selected from



R^{10} is H, C(=O)R¹⁷, C(=O)OR¹⁷;

C₁-C₄ alkyl optionally substituted with 0-1 R^{10a};

phenyl substituted with 0-4 R^{10b};

C₃-C₆ carbocycle substituted with 0-3 R^{10b}; or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a} is selected from H, C₁-C₄ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b} , at each occurrence, is independently selected from H, OH, C₁-C₄ alkyl, C₁-C₃ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, or CF₃;

R^{11} is selected from

H, C₁-C₄ alkoxy, Cl, F, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷, CF₃;

C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 40 of 89 C_6-C_{10} aryl substituted with 0-3 R^{11b} ; C_3-C_6 carbocycle substituted with 0-3 R^{11b} ; or5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b} ; R^{11a} , at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14} , F, =O, $NR^{15}R^{16}$, CF_3 , or phenyl substituted with 0-3 R^{11b} ; R^{11b} , at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3 , C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;Z is C_1-C_4 alkyl substituted with 1-3 R^{12} ; C_2-C_4 alketyl substituted with 1-3 R^{12} ; C_2-C_4 alkynyl substituted with 1-3 R^{12} ; C_6-C_{10} aryl substituted with 0-4 R^{12b} ; C_3-C_6 carbocycle substituted with 0-4 R^{12b} ; or5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b} ; R^{12} , at each occurrence, is independently selected from C_6-C_{10} aryl substituted with 0-4 R^{12b} ; C_3-C_6 carbocycle substituted with 0-4 R^{12b} ; or5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b} ; R^{12b} , at each occurrence, is independently selected fromH, OH, Cl, F, $NR^{15}R^{16}$, CF_3 , acetyl, SCH_3 , $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy; R^{13} , at each occurrence, is independently selected fromH, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2 , $NR^{15}R^{16}$, and CF_3 ;

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 41 of 89*

R^{14} is H, phenyl, benzyl, C₁-C₄ alkyl, or C₂-C₄ alkoxyalkyl;

R^{15} , at each occurrence, is independently selected from H, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)2-;

R^{16} , at each occurrence, is independently selected from
H, OH, C₁-C₄ alkyl, benzyl, phenethyl,
(C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)2-;

R^{17} is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl,
ethoxyethyl,
phenyl substituted by 0-3 R^{17a} , or
-CH₂-phenyl substituted by 0-3 R^{17a} ;

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

R^{18} , at each occurrence, is independently selected from
H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

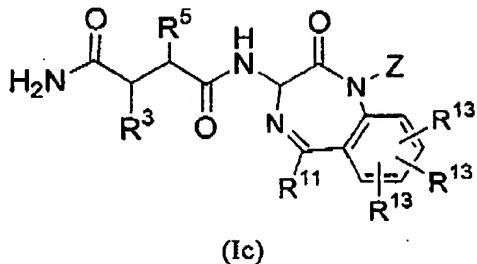
R^{19} , at each occurrence, is independently selected from
H, methyl, and ethyl;

provided, when R^{13} is H,
then Z is butyl substituted with 1-3 R^{12} ;
C₂-C₄ alkenyl substituted with 1-3 R^{12} ; or
C₂-C₄ alkynyl substituted with 1-3 R^{12} .

15. (CANCELLED)

16. (CURRENTLY AMENDED) A compound according to Claim 14 of Formula (Ic):

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 42 of 89

or a pharmaceutically acceptable salt thereof
wherein

R^3 is R^4 ,

R^4 is C₁-C₄ alkyl substituted with 0-1 R^{4a} ,
C₂-C₄ alkenyl substituted with 0-1 R^{4a} , or
C₂-C₄ alkynyl substituted with 0-1 R^{4a} ;

R^{4a} is selected from
H, F, CF₃,
C₃-C₆ carbocycle substituted with 0-3 R^{4b} ,
phenyl substituted with 0-3 R^{4b} , or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b} ; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{4b} , at each occurrence, is independently selected from H, OH, Cl, F, NR₁₅R₁₆, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R^5 is C₁-C₄ alkyl substituted with 0-1 R^{5b} ;
C₂-C₄ alkenyl substituted with 0-1 R^{5b} ;
C₂-C₄ alkynyl substituted with 0-1 R^{5b} ;

R^{5b} is selected from:

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 43 of 89*

H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, =O;
C₃-C₆ carbocycle substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹¹ is selected from
H, NR¹⁸R¹⁹, CF₃;
C₁-C₄ alkyl optionally substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
C₃-C₆ carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a} is selected from H, C₁-C₄ alkyl, OR¹⁴, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

Z is C₁-C₃ alkyl substituted with 1-3 R¹²;
C₂-C₃ alkenyl substituted with 1-3 R¹²;
C₂-C₃ alkynyl substituted with 1-3 R¹²;
C₆-C₁₀ aryl substituted with 0-4 R^{12b};

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 44 of 89

C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R¹², at each occurrence, is independently selected from
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{12b}, at each occurrence, is independently selected from
H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from
H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R¹⁶, at each occurrence, is independently selected from
H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-S(=O)₂-, and ethyl-S(=O)₂-;

R¹⁸, at each occurrence, is independently selected from
H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 45 of 89

R^{19} , at each occurrence, is independently selected from
H, methyl, and ethyl;

provided, when R^{13} is H,
then Z is C₂-C₃ alkenyl substituted with 1-3 R^{12} ; or
C₂-C₃ alkynyl substituted with 1-3 R^{12} .

17. – 19. (Canceled)

20. (PREVIOUSLY PRESENTED) A compound according to Claim 16, wherein:

R^3 is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH₂CH₂CH₂CH₃,
-CH(CH₃)₂, -CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂,
-CH₂CF₃, -CH₂CH₂CF₃, -CH₂CH₂CH₂CF₃,
-CH=CH₂, -CH₂CH=CH₂, -CH₂C(CH₃)=CH₂,
-CH₂CH₂CH=CH₂,
cis-CH₂CH=CH(CH₃),
trans-CH₂CH=CH(CH₃),
-C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃),
cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-, cyclohexyl-CH₂-, cyclopropyl-CH₂CH₂-,
cyclobutyl-CH₂CH₂-, cyclopentyl-CH₂CH₂-,
cyclohexyl-CH₂CH₂-, phenyl-CH₂-,
(2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-, (4-F-phenyl)CH₂-,
(2-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂-,
(2,3-diF-phenyl)CH₂-, (2,4-diF-phenyl)CH₂-,
(2,5-diF-phenyl)CH₂-, (2,6-diF-phenyl)CH₂-,
(3,4-diF-phenyl)CH₂-, (3,5-diF-phenyl)CH₂-,
(2,3-diCl-phenyl)CH₂-, (2,4-diCl-phenyl)CH₂-,
(2,5-diCl-phenyl)CH₂-, (2,6-diCl-phenyl)CH₂-,
(3,4-diCl-phenyl)CH₂-, (3,5-diCl-phenyl)CH₂-,
(3-F-4-Cl-phenyl)CH₂-, (3-F-5-Cl-phenyl)CH₂-,

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 46 of 89

(3-Cl-4-F-phenyl)CH₂-, phenyl-CH₂CH₂-,
(2-F-phenyl)CH₂CH₂-, (3-F-phenyl)CH₂CH₂-,
(4-F-phenyl)CH₂CH₂-, (2-Cl-phenyl)CH₂CH₂-,
(3-Cl-phenyl)CH₂CH₂-, (4-Cl-phenyl)CH₂CH₂-,
(2,3-diF-phenyl)CH₂CH₂-, (2,4-diF-phenyl)CH₂CH₂-,
(2,5-diF-phenyl)CH₂CH₂-, (2,6-diF-phenyl)CH₂CH₂-,
(3,4-diF-phenyl)CH₂CH₂-, (3,5-diF-phenyl)CH₂CH₂-,
(2,3-diCl-phenyl)CH₂CH₂-, (2,4-diCl-phenyl)CH₂CH₂-,
(2,5-diCl-phenyl)CH₂CH₂-, (2,6-diCl-phenyl)CH₂CH₂-,
(3,4-diCl-phenyl)CH₂CH₂-, (3,5-diCl-phenyl)CH₂CH₂-,
(3-F-4-Cl-phenyl)CH₂CH₂-, or (3-F-5-Cl-phenyl)CH₂CH₂-,

R⁵ is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH(CH₃)₂, -CH₂CH₂CH₂CH₃,
-CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂, -CH₂C(CH₃)₃,
-CH₂CH₂CH₂CH₂CH₃, -CH(CH₃)CH₂CH₂CH₃, -CH₂CH(CH₃)CH₂CH₃,
-CH₂CH₂CH(CH₃)₂, -CH(CH₂CH₃)₂, -CH₂CF₃, -CH₂CH₂CF₃,
-CH₂CH₂CH₂CF₃, -CH₂CH₂CH₂CH₂CF₃, -CH=CH₂, -CH₂CH=CH₂,
-CH=CHCH₃, cis-CH₂CH=CH(CH₃), trans-CH₂CH=CH(CH₃),
trans-CH₂CH=CH(C₆H₅), -CH₂CH=C(CH₃)₂, cis-CH₂CH=CHCH₂CH₃,
trans-CH₂CH=CHCH₂CH₃, cis-CH₂CH₂CH=CH(CH₃),
trans-CH₂CH₂CH=CH(CH₃), trans-CH₂CH=CHCH₂(C₆H₅),
-C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃), -CH₂C≡C(C₆H₅),
-CH₂CH₂C≡CH, -CH₂CH₂C≡C(CH₃), -CH₂CH₂C≡C(C₆H₅),
cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-,
cyclohexyl-CH₂-, (2-CH₃-cyclopropyl)CH₂-,
(3-CH₃-cyclobutyl)CH₂-,
cyclopropyl-CH₂CH₂-, cyclobutyl-CH₂CH₂-,
cyclopentyl-CH₂CH₂-, cyclohexyl-CH₂CH₂-,
(2-CH₃-cyclopropyl)CH₂CH₂-, (3-CH₃-cyclobutyl)CH₂CH₂-,
phenyl-CH₂-, (2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-,
(4-F-phenyl)CH₂-, furanyl-CH₂-, thienyl-CH₂-,
pyridyl-CH₂-, 1-imidazolyl-CH₂-, oxazolyl-CH₂-,
isoxazolyl-CH₂-,
phenyl-CH₂CH₂-, (2-F-phenyl)CH₂CH₂-, (3-F-phenyl)CH₂CH₂-,

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 47 of 89

(4-F-phenyl)CH₂CH₂-, furanyl-CH₂CH₂-, thienyl-CH₂CH₂-,
pyridyl-CH₂CH₂-, 1-imidazolyl-CH₂CH₂-, oxazolyl-CH₂CH₂-,
isoxazolyl-CH₂CH₂-;

Z is phenyl, 2-F-phenyl, 3-F-phenyl, 4-F-phenyl,
2-Cl-phenyl, 3-Cl-phenyl, 4-Cl-phenyl, 2,3-diF-phenyl,
2,4-diF-phenyl, 2,5-diF-phenyl, 2,6-diF-phenyl,
3,4-diF-phenyl, 3,5-diF-phenyl, 2,3-diCl-phenyl,
2,4-diCl-phenyl, 2,5-diCl-phenyl, 2,6-diCl-phenyl,
3,4-diCl-phenyl, 3,5-diCl-phenyl, 3-F-4-Cl-phenyl,
3-F-5-Cl-phenyl, 3-Cl-4-F-phenyl, 2-MeO-phenyl,
3-MeO-phenyl, 4-MeO-phenyl, 2-Me-phenyl, 3-Me-phenyl,
4-Me-phenyl, 2-MeS-phenyl, 3-MeS-phenyl, 4-MeS-phenyl,
2-CF₃O-phenyl, 3-CF₃O-phenyl, 4-CF₃O-phenyl,
furanyl, thienyl, pyridyl, 2-Me-pyridyl, 3-Me-pyridyl,
4-Me-pyridyl, 1-imidazolyl, oxazolyl, isoxazolyl,
cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl,
N-piperidinyl,
phenyl-CH₂-, (2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-,
(4-F-phenyl)CH₂-, (2-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂-, (2,3-diF-phenyl)CH₂-,
(2,4-diF-phenyl)CH₂-, (2,5-diF-phenyl)CH₂-,
(2,6-diF-phenyl)CH₂-, (3,4-diF-phenyl)CH₂-,
(3,5-diF-phenyl)CH₂-, (2,3-diCl-phenyl)CH₂-,
(2,4-diCl-phenyl)CH₂-, (2,5-diCl-phenyl)CH₂-,
(2,6-diCl-phenyl)CH₂-, (3,4-diCl-phenyl)CH₂-,
(3,5-diCl-phenyl)CH₂-, (3-F-4-Cl-phenyl)CH₂-,
(3-F-5-Cl-phenyl)CH₂-, (3-Cl-4-F-phenyl)CH₂-,
(2-MeO-phenyl)CH₂-, (3-MeO-phenyl)CH₂-,
(4-MeO-phenyl)CH₂-, (2-Me-phenyl)CH₂-,
(3-Me-phenyl)CH₂-, (4-Me-phenyl)CH₂-,
(2-MeS-phenyl)CH₂-, (3-MeS-phenyl)CH₂-,
(4-MeS-phenyl)CH₂-, (2-CF₃O-phenyl)CH₂-,
(3-CF₃O-phenyl)CH₂-, (4-CF₃O-phenyl)CH₂-,

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 48 of 89

(furanyl)CH₂-, (thienyl)CH₂-, (pyridyl)CH₂-,
(2-Me-pyridyl)CH₂-, (3-Me-pyridyl)CH₂-,
(4-Me-pyridyl)CH₂-, (1-imidazolyl)CH₂-,
(oxazolyl)CH₂-, (isoxazolyl)CH₂-,
(cyclopropyl)CH₂-, (cyclobutyl)CH₂-, (cyclopentyl)CH₂-,
(cyclohexyl)CH₂-, (N-piperidinyl)CH₂-,

phenyl-CH₂CH₂-, (phenyl)₂CHCH₂-, (2-F-phenyl)CH₂CH₂-,
(3-F-phenyl)CH₂CH₂-, (4-F-phenyl)CH₂CH₂-,
(2-Cl-phenyl)CH₂CH₂-, (3-Cl-phenyl)CH₂CH₂-,
(4-Cl-phenyl)CH₂CH₂-, (2,3-diF-phenyl)CH₂CH₂-,
(2,4-diF-phenyl)CH₂CH₂-, (2,5-diF-phenyl)CH₂CH₂-,
(2,6-diF-phenyl)CH₂CH₂-, (3,4-diF-phenyl)CH₂CH₂-,
(3,5-diF-phenyl)CH₂CH₂-, (2,3-diCl-phenyl)CH₂CH₂-,
(2,4-diCl-phenyl)CH₂CH₂-, (2,5-diCl-phenyl)CH₂CH₂-,
(2,6-diCl-phenyl)CH₂CH₂-, (3,4-diCl-phenyl)CH₂CH₂-,
(3,5-diCl-phenyl)CH₂CH₂-, (3-F-4-Cl-phenyl)CH₂CH₂-,
(3-F-5-Cl-phenyl)CH₂CH₂-, (3-Cl-4-F-phenyl)CH₂CH₂-,
(2-MeO-phenyl)CH₂CH₂-, (3-MeO-phenyl)CH₂CH₂-,
(4-MeO-phenyl)CH₂CH₂-, (2-Me-phenyl)CH₂CH₂-,
(3-Me-phenyl)CH₂CH₂-, (4-Me-phenyl)CH₂CH₂-,
(2-MeS-phenyl)CH₂CH₂-, (3-MeS-phenyl)CH₂CH₂-,
(4-MeS-phenyl)CH₂CH₂-, (2-CF₃O-phenyl)CH₂CH₂-,
(3-CF₃O-phenyl)CH₂CH₂-, (4-CF₃O-phenyl)CH₂CH₂-, (furanyl)CH₂CH₂-
, (thienyl)CH₂CH₂-, (pyridyl)CH₂CH₂-,
(2-Me-pyridyl)CH₂CH₂-, (3-Me-pyridyl)CH₂CH₂-,
(4-Me-pyridyl)CH₂CH₂-, (imidazolyl)CH₂CH₂-, (oxazolyl)CH₂CH₂-,
(isoxazolyl)CH₂CH₂-, (cyclopropyl)CH₂CH₂-, (cyclobutyl)CH₂CH₂-,
(cyclopentyl)CH₂CH₂-, (cyclohexyl)CH₂CH₂-, or
(N-piperidinyl)CH₂CH₂-,

R¹⁰ is H, methyl, ethyl, phenyl, benzyl, phenethyl,
4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,
4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 49 of 89*

4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,
4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, or
(4-CF₃-phenyl)CH₂CH₂-;

R¹¹, at each occurrence, is independently selected from

H, methyl, ethyl, phenyl, benzyl, phenethyl,
4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,
3-F-phenyl, (3-F-phenyl)CH₂-, (3-F-phenyl)CH₂CH₂-,
2-F-phenyl, (2-F-phenyl)CH₂-, (2-F-phenyl)CH₂CH₂-,
4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,
3-Cl-phenyl, (3-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂CH₂-,
4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,
3-CH₃-phenyl, (3-CH₃-phenyl)CH₂-, (3-CH₃-phenyl)CH₂CH₂-,
4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, (4-CF₃-phenyl)CH₂CH₂-,
pyrid-2-yl, pyrid-3-yl, or pyrid-4-yl, and

R¹³, at each occurrence, is independently selected from
H, F, Cl, OH, -CH₃, -CH₂CH₃, -OCH₃, or -CF₃.

21. (CANCELLED)

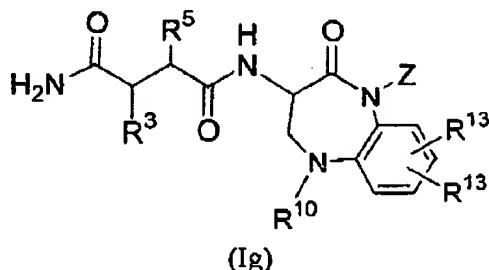
22. (ORIGINAL) A pharmaceutical composition comprising a compound of Claim 1; and a pharmaceutically acceptable carrier.

23. (PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 1.

24. (CANCELLED)

25. (PREVIOUSLY PRESENTED) A compound according to Claim 4 of Formula (Ig):

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 50 of 89

or a pharmaceutically acceptable salt thereof wherein:

R³ is R⁴,R⁴ is C₁-C₄ alkyl substituted with 0-1 R^{4a},C₂-C₄ alkenyl substituted with 0-1 R^{4a}, or
C₂-C₄ alkynyl substituted with 0-1 R^{4a};R^{4a}, at each occurrence, is independently selected fromH, F, CF₃,C₃-C₆ carbocycle substituted with 0-3 R^{4b},phenyl substituted with 0-3 R^{4b}, or5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;R⁵ is C₁-C₄ alkyl substituted with 0-1 R^{5b};C₂-C₄ alkenyl substituted with 0-1 R^{5b};C₂-C₄ alkynyl substituted with 0-1 R^{5b};R^{5b} is selected from:H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, =O;

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action

Mailed 04/08/2005

Page 51 of 89

C₃-C₆ carbocycle substituted with 0-2 R^{5c};

phenyl substituted with 0-3 R^{5c}; or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷;

C₁-C₄ alkyl optionally substituted with 0-1 R^{10a};

phenyl substituted with 0-4 R^{10b};

C₃-C₆ carbocycle substituted with 0-3 R^{10b}; or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{10b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{10a} is selected from H, methyl, ethyl, propyl, butyl, OR¹⁴, Cl, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, Cl, F, NR¹⁵R¹⁶, and CF₃;

Z is H;

C₁-C₄ alkyl substituted with 0-3 R^{12a};

C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or

C₂-C₄ alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action

Mailed 04/08/2005

Page 52 of 89

H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from

H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R¹⁶, at each occurrence, is independently selected from

H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-S(=O)₂-, and ethyl-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl,

phenyl substituted by 0-3 R^{17a}, or

-CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or -OCF₃;

R¹⁸, at each occurrence, is independently selected from

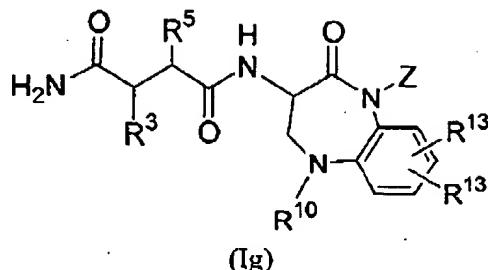
H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from

H, methyl, and ethyl.

26. (CURRENTLY AMENDED) A compound according to Claim 14 of Formula (Ig):

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 53 of 89

or a pharmaceutically acceptable salt thereof wherein:

R³ is R⁴,R⁴ is C₁-C₄ alkyl substituted with 0-1 R^{4a},C₂-C₄ alkenyl substituted with 0-1 R^{4a}, orC₂-C₄ alkynyl substituted with 0-1 R^{4a};R^{4a} is selected fromH, F, CF₃,C₃-C₆ carbocycle substituted with 0-3 R^{4b},phenyl substituted with 0-3 R^{4b}, or5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;R⁵ is C₁-C₄ alkyl substituted with 0-1 R^{5b};C₂-C₄ alkenyl substituted with 0-1 R^{5b};C₂-C₄ alkynyl substituted with 0-1 R^{5b};R^{5b} is selected from:H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, =O;

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 54 of 89*

C₃-C₆ carbocycle substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thieryl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷;
C₁-C₄ alkyl optionally substituted with 0-1 R^{10a};
phenyl substituted with 0-4 R^{10b};
C₃-C₆ carbocycle substituted with 0-3 R^{10b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{10b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thieryl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{10a} is selected from H, methyl, ethyl, propyl, butyl, OR¹⁴, Cl, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, Cl, F, NR¹⁵R¹⁶, and CF₃;

Z is C₁-C₃ alkyl substituted with 1-3 R¹²;
C₂-C₃ alkenyl substituted with 1-3 R¹²;
C₂-C₃ alkynyl substituted with 1-3 R¹²;
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 55 of 89*

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R¹², at each occurrence, is independently selected from

C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{12b}, at each occurrence, is independently selected from

H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from

H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R¹⁶, at each occurrence, is independently selected from

H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-S(=O)₂-, and ethyl-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl,
phenyl substituted by 0-3 R^{17a}, or
-CH₂-phenyl substituted by 0-3 R^{17a};

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 56 of 89*

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF_3 , or OCF_3 ;

R^{18} , at each occurrence, is independently selected from
H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R^{19} , at each occurrence, is independently selected from
H, methyl, and ethyl;

provided, when R^{13} is H,
then Z is C₂-C₃ alkenyl substituted with 1-3 R^{12} ; or
C₂-C₃ alkynyl substituted with 1-3 R^{12} .

27. **(PREVIOUSLY PRESENTED)** A pharmaceutical composition comprising a compound according to Claim 2 and a pharmaceutically acceptable carrier.
28. **(PREVIOUSLY PRESENTED)** A pharmaceutical composition comprising a compound according to Claim 3 and a pharmaceutically acceptable carrier.
29. **(PREVIOUSLY PRESENTED)** A pharmaceutical composition comprising a compound according to Claim 4 and a pharmaceutically acceptable carrier.
30. **(PREVIOUSLY PRESENTED)** A pharmaceutical composition comprising a compound according to Claim 6 and a pharmaceutically acceptable carrier.
31. - 32. **(CANCELLED)**
33. **(PREVIOUSLY PRESENTED)** A pharmaceutical composition comprising a compound according to Claim 11 and a pharmaceutically acceptable carrier.
34. **(CANCELLED)**
35. **(PREVIOUSLY PRESENTED)** A pharmaceutical composition comprising a compound according to Claim 13 and a pharmaceutically acceptable carrier.

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 57 of 89*

36. **(PREVIOUSLY PRESENTED)** A pharmaceutical composition comprising a compound according to Claim 14 and a pharmaceutically acceptable carrier.
37. **(PREVIOUSLY PRESENTED)** A pharmaceutical composition comprising a compound according to Claim 16 and a pharmaceutically acceptable carrier.
38. **(CANCELLED)**
39. **(PREVIOUSLY PRESENTED)** A pharmaceutical composition comprising a compound according to Claim 20 and a pharmaceutically acceptable carrier.
40. **(PREVIOUSLY PRESENTED)** A pharmaceutical composition comprising a compound according to Claim 25 and a pharmaceutically acceptable carrier.
41. **(PREVIOUSLY PRESENTED)** A pharmaceutical composition comprising a compound according to Claim 26 and a pharmaceutically acceptable carrier.
42. **(PREVIOUSLY PRESENTED)** A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 2.
43. **(PREVIOUSLY PRESENTED)** A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 3.
44. **(PREVIOUSLY PRESENTED)** A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 4.
45. **(PREVIOUSLY PRESENTED)** A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 6.

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 58 of 89*

46.- 47. (CANCELLED)

48. (PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 11.

49. (CANCELLED)

50. (PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 13.

51. (PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 14.

52. (PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 16.

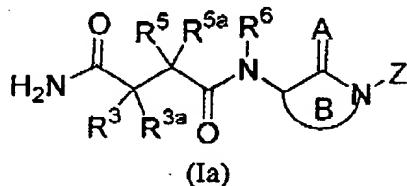
53. (CANCELLED)

54. (PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 20.

55. (PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 25.

56. (PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 26.

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 59 of 89**57. (CURRENTLY AMENDED)** A compound according to Claim 2 of Formula (Ia)

or a pharmaceutically acceptable salt thereof,
wherein:

R^3 is $-(CR^7R^{7a})_n-R^4$,
 $-(CR^7R^{7a})_n-S-(CR^7R^{7a})_m-R^4$,
 $-(CR^7R^{7a})_n-O-(CR^7R^{7a})_m-R^4$, or
 $-(CR^7R^{7a})_n-N(R^{7b})-(CR^7R^{7a})_m-R^4$;

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R^4 is H, OH, OR^{14a},
C₁-C₆ alkyl substituted with 0-3 R^{4a},
C₂-C₆ alkenyl substituted with 0-3 R^{4a},
C₂-C₆ alkynyl substituted with 0-3 R^{4a},
C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,

CT01/HOFF/HAA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 60 of 89

C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
 C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁵ is H, OR¹⁴;
 C₁-C₆ alkyl substituted with 0-3 R^{5b};
 C₁-C₆ alkoxy substituted with 0-3 R^{5b};
 C₂-C₆ alkenyl substituted with 0-3 R^{5b};
 C₂-C₆ alkynyl substituted with 0-3 R^{5b};
 C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
 C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5a} is H or C₁-C₄ alkyl;

R^{5b}, at each occurrence, is independently selected from:
 H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶,
 C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
 C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

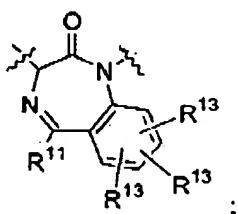
R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 61 of 89R⁶ is H, methyl, or ethyl;R⁷, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl and C₁-C₄ alkyl;R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is



R¹¹, at each occurrence, is independently selected from
 H, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷,
 C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, CF₃;
 C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};
 C₆-C₁₀ aryl substituted with 0-3 R^{11b};
 C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 62 of 89*

H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

Z is H;

C₁-C₆ alkyl substituted with 0-3 R^{12a};
C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or
C₂-C₄ alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R¹³, at each occurrence, is independently selected from

H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from

H, OH, C₁-C₆ alkyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,

aryl substituted by 0-4 R^{17a}, or
-CH₂-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

R¹⁸, at each occurrence, is independently selected from

CT01/HOFFHA/216624.1

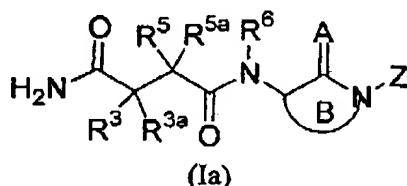
U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 63 of 89*

H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)2-; and

R¹⁹, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-.

58. (CURRENTLY AMENDED) A compound according to Claim 2 of Formula (Ia)



or a pharmaceutically acceptable salt thereof, wherein:

R^3 is $-(CR^7R^7a)_{n-R^4}$,
 $-(CR^7R^7a)_{n-S-(CR^7R^7a)_{m-R^4}}$,
 $-(CR^7R^7a)_{n-O-(CR^7R^7a)_{m-R^4}}$, or
 $-(CR^7R^7a)_{n-N(R^7b)-(CR^7R^7a)_{m-R^4}}$.

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R^4 is H, OH, OR^{14a},

C₁-C₆ alkyl substituted with 0-3 R^{4a},
C₂-C₆ alkenyl substituted with 0-3 R^{4a},
C₂-C₆ alkynyl substituted with 0-3 R^{4a},
C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},

U.S. Appl. No. 09/505,788, filed Feb 17, 2005

Response to Final Office Action

Mailed 04/08/2005

Page 64 of 89

 $\text{C}_6\text{-C}_{10}$ aryl substituted with 0-3 R^{4b} , or5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b} ; R^{4a} , at each occurrence, is independently selected from H, F, Cl, Br, I, CF_3 , $\text{C}_3\text{-C}_{10}$ carbocycle substituted with 0-3 R^{4b} , $\text{C}_6\text{-C}_{10}$ aryl substituted with 0-3 R^{4b} , or5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b} ; R^{4b} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2 , $\text{NR}^{15}\text{R}^{16}$, CF_3 , acetyl, SCH_3 , $\text{S}(\text{=O})\text{CH}_3$, $\text{S}(\text{=O})_2\text{CH}_3$, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_4$ alkoxy, $\text{C}_1\text{-C}_4$ haloalkyl, and $\text{C}_1\text{-C}_4$ haloalkoxy; R^5 is H, OR^{14} ; $\text{C}_1\text{-C}_6$ alkyl substituted with 0-3 R^{5b} ; $\text{C}_1\text{-C}_6$ alkoxy substituted with 0-3 R^{5b} ; $\text{C}_2\text{-C}_6$ alkenyl substituted with 0-3 R^{5b} ; $\text{C}_2\text{-C}_6$ alkyanyl substituted with 0-3 R^{5b} ; $\text{C}_3\text{-C}_{10}$ carbocycle substituted with 0-3 R^{5c} ; $\text{C}_6\text{-C}_{10}$ aryl substituted with 0-3 R^{5c} ; or5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c} ; R^{5a} is H or $\text{C}_1\text{-C}_4$ alkyl; R^{5b} , at each occurrence, is independently selected from:H, $\text{C}_1\text{-C}_6$ alkyl, CF_3 , OR^{14} , Cl, F, Br, I, NO_2 , $\text{NR}^{15}\text{R}^{16}$, $\text{C}_3\text{-C}_{10}$ carbocycle substituted with 0-3 R^{5c} ; $\text{C}_6\text{-C}_{10}$ aryl substituted with 0-3 R^{5c} ; or

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 65 of 89

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

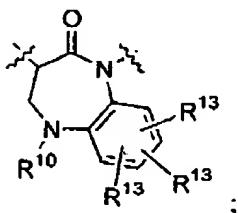
R⁶ is H, methyl, or ethyl;

R⁷, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl and C₁-C₄ alkyl;

R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is



R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹,

S(=O)₂NR¹⁸R¹⁹, S(=O)₂R¹⁷;

C₁-C₆ alkyl optionally substituted with 0-2 R^{10a};

C₆-C₁₀ aryl substituted with 0-4 R^{10b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{10b}; or

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 66 of 89*

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, or CF₃;

Z is H;

C₁-C₆ alkyl substituted with 0-3 R^{12a};
C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or
C₂-C₄ alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R¹³, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 67 of 89

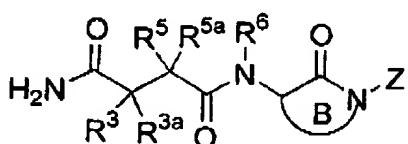
aryl substituted by 0-4 R^{17a}, or
 -CH₂-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

R¹⁸, at each occurrence, is independently selected from
 H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
 (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-; and

R¹⁹, at each occurrence, is independently selected from
 H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
 (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-.

59. (CURRENTLY AMENDED) A compound according to Claim 12 of Formula (Ia'')



(Ia'')

or a pharmaceutically acceptable salt thereof,
 wherein:

R³ is -(CR⁷R^{7a})_n-R⁴,
 -(CR⁷R^{7a})_n-S-(CR⁷R^{7a})_m-R⁴,
 -(CR⁷R^{7a})_n-O-(CR⁷R^{7a})_m-R⁴, or
 -(CR⁷R^{7a})_n-N(R^{7b})-(CR⁷R^{7a})_m-R⁴;

n is 0, 1, or 2;

m is 0, 1, or 2;

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 68 of 89

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},

C₁-C₆ alkyl substituted with 0-3 R^{4a},

C₂-C₆ alkenyl substituted with 0-3 R^{4a},

C₂-C₆ alkynyl substituted with 0-3 R^{4a},

C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},

C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,

C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},

C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,

NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy,

C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁵ is H, OR¹⁴;

C₁-C₆ alkyl substituted with 0-3 R^{5b};

C₁-C₆ alkoxy substituted with 0-3 R^{5b};

C₂-C₆ alkenyl substituted with 0-3 R^{5b};

C₂-C₆ alkynyl substituted with 0-3 R^{5b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};

C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 69 of 89

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5a} is H or C₁-C₄ alkyl;

R^{5b}, at each occurrence, is independently selected from:

H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶;

C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};

C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁶ is H, methyl, or ethyl;

R⁷, at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl, and C₁-C₄ alkyl;

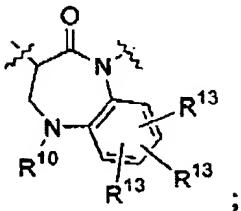
R^{7a}, at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 70 of 89

R10 is H, C(=O)R17, C(=O)OR17, C(=O)NR18R19,

S(=O)2NR18R19, S(=O)2R17;

C1-C6 alkyl optionally substituted with 0-2 R10a;

C6-C10 aryl substituted with 0-4 R10b;

C3-C10 carbocycle substituted with 0-3 R10b; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R10b;

R10a, at each occurrence, is independently selected from H, C1-C6 alkyl, OR14, Cl, F, Br, I, =O, CN, NO2, NR15R16, CF3, or phenyl substituted with 0-4 R10b;

R10b, at each occurrence, is independently selected from H, OH, C1-C6 alkyl, C1-C4 alkoxy, Cl, F, Br, I, CN, NO2, NR15R16, or CF3;

Z is C1-C6 alkyl substituted with 1-3 R12;

C2-C4 alkenyl substituted with 1-3 R12;

C2-C4 alkynyl substituted with 1-3 R12;

C6-C10 aryl substituted with 0-4 R12b;

C3-C10 carbocycle substituted with 0-4 R12b; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R12b;

R12, at each occurrence, is independently selected from

C6-C10 aryl substituted with 0-4 R12b;

C3-C10 carbocycle substituted with 0-4 R12b; or

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 71 of 89*

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R¹³, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl, aryl substituted by 0-4 R^{17a}, or -CH₂-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

R¹⁸, at each occurrence, is independently selected from H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-; and

R¹⁹, at each occurrence, is independently selected from

CT01/HOFFHA/216624.1

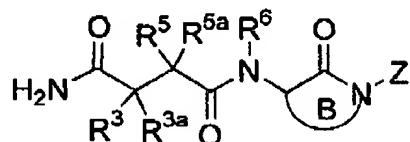
U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 72 of 89

H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)2-;

provided, when R¹³ is H,
then Z is C₄-C₆ alkyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²; or
C₂-C₄ alkynyl substituted with 1-3 R¹².

60. (CURRENTLY AMENDED) A compound according to Claim 12 of Formula (Ia'')



(Ia'')

or a pharmaceutically acceptable salt thereof,
wherein:

R³ is -(CR⁷R^{7a})_n-R⁴,
-(CR⁷R^{7a})_n-S-(CR⁷R^{7a})_m-R⁴,
-(CR⁷R^{7a})_n-O-(CR⁷R^{7a})_m-R⁴, or
-(CR⁷R^{7a})_n-N(R^{7b})-(CR⁷R^{7a})_m-R⁴;

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 73 of 89*

C₁-C₆ alkyl substituted with 0-3 R^{4a};
C₂-C₆ alkenyl substituted with 0-3 R^{4a};
C₂-C₆ alkynyl substituted with 0-3 R^{4a};
C₃-C₁₀ carbocycle substituted with 0-3 R^{4b};
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃, C₃-C₁₀ carbocycle substituted with 0-3 R^{4b}, C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁵ is H, OR¹⁴;
C₁-C₆ alkyl substituted with 0-3 R^{5b};
C₁-C₆ alkoxy substituted with 0-3 R^{5b};
C₂-C₆ alkenyl substituted with 0-3 R^{5b};
C₂-C₆ alkynyl substituted with 0-3 R^{5b};
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
C₆-C₁₀ aryl substituted with 0-3 R^{5c}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5a} is H or C₁-C₄ alkyl;

R^{5b}, at each occurrence, is independently selected from:

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 74 of 89

H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶,
 C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
 C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

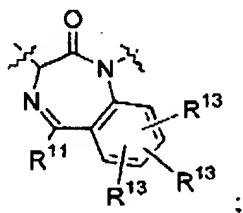
R⁶ is H, methyl, or ethyl;

R⁷, at each occurrence, is independently selected from
 H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl, and C₁-C₄ alkyl;

R^{7a}, at each occurrence, is independently selected from
 H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is



R¹¹, at each occurrence, is independently selected from
 H, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, CF₃;
 C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 75 of 89*

C₆-C₁₀ aryl substituted with 0-3 R^{11b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

Z is C₁-C₆ alkyl substituted with 1-3 R¹²;

C₂-C₄ alkenyl substituted with 1-3 R¹²;

C₂-C₄ alkynyl substituted with 1-3 R¹²;

C₆-C₁₀ aryl substituted with 0-4 R^{12b};

C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R¹², at each occurrence, is independently selected from

C₆-C₁₀ aryl substituted with 0-4 R^{12b};

C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R¹³, at each occurrence, is independently selected from

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 76 of 89*

H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)2-;

R¹⁶, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)2-;

R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,
aryl substituted by 0-4 R^{17a}, or
-CH₂-aryl substituted by 0-4 R^{17a};

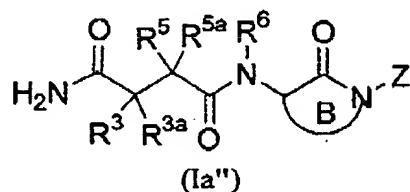
R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

R¹⁸, at each occurrence, is independently selected from
H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)2-; and

R¹⁹, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)2-;

provided, when R¹³ is H,
then Z is C₄-C₆ alkyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²; or
C₂-C₄ alkynyl substituted with 1-3 R¹².

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 77 of 89**61. (CURRENTLY AMENDED)** A compound according to Claim 13 of Formula (Ia'')

or a pharmaceutically acceptable salt thereof,
wherein:

R³ is -(CHR⁷)_n-R⁴,

n is 0 or 1;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},

C₁-C₄ alkyl substituted with 0-2 R^{4a},

C₂-C₄ alkenyl substituted with 0-2 R^{4a},

C₂-C₄ alkynyl substituted with 0-1 R^{4a},

C₃-C₆ carbocycle substituted with 0-3 R^{4b},

C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,

oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,

C₃-C₆ carbocycle substituted with 0-3 R^{4b},

phenyl substituted with 0-3 R^{4b}, or

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 78 of 89

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is H, OR¹⁴;
C₁-C₄ alkyl substituted with 0-3 R^{5b};
C₂-C₄ alkenyl substituted with 0-3 R^{5b};
C₂-C₄ alkynyl substituted with 0-3 R^{5b};

R^{5a} is H, methyl, ethyl, propyl, or butyl;

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, Cl, F, Br, I, =O;
C₃-C₆ carbocycle substituted with 0-3 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c};

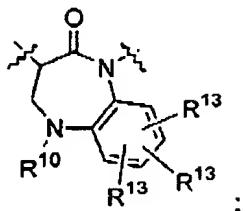
R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁶ is H;

R⁷, at each occurrence, is independently selected from H, F, CF₃, methyl, and ethyl;

Ring B is

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 79 of 89R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷;C₁-C₄ alkyl optionally substituted with 0-1 R^{10a};phenyl substituted with 0-4 R^{10b};C₃-C₆ carbocycle substituted with 0-3 R^{10b}; or5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{10b};R^{10a} is selected from H, C₁-C₄ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};R^{10b}, at each occurrence, is independently selected from H, OH, C₁-C₄ alkyl, C₁-C₃ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, or CF₃;Z is C₁-C₄ alkyl substituted with 1-3 R¹²;C₂-C₄ alkenyl substituted with 1-3 R¹²;C₂-C₄ alkynyl substituted with 1-3 R¹²;C₆-C₁₀ aryl substituted with 0-4 R^{12b};C₃-C₆ carbocycle substituted with 0-4 R^{12b}; or5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b};R¹², at each occurrence, is independently selected fromC₆-C₁₀ aryl substituted with 0-4 R^{12b};C₃-C₆ carbocycle substituted with 0-4 R^{12b}; or

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 80 of 89*

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₄ alkyl, or C₂-C₄ alkoxyalkyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from H, OH, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl, phenyl substituted by 0-3 R^{17a}, or -CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

R¹⁸, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from H, methyl, and ethyl;

provided, when R¹³ is H,

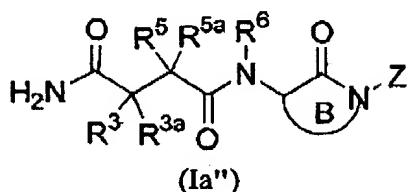
CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 81 of 89

then Z is butyl substituted with 1-3 R¹²;
 C₂-C₄ alkenyl substituted with 1-3 R¹²; or
 C₂-C₄ alkynyl substituted with 1-3 R¹².

62. (CURRENTLY AMENDED) A compound according to Claim 13 of Formula (Ia'')



or a pharmaceutically acceptable salt thereof,
 wherein:

R³ is -(CHR⁷)_n-R⁴,

n is 0 or 1;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},
 C₁-C₄ alkyl substituted with 0-2 R^{4a},
 C₂-C₄ alkenyl substituted with 0-2 R^{4a},
 C₂-C₄ alkynyl substituted with 0-1 R^{4a},
 C₃-C₆ carbocycle substituted with 0-3 R^{4b},
 C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,

CT01/HOFFHA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 82 of 89*

C₃-C₆ carbocycle substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,
NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy,
C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is H, OR¹⁴;
C₁-C₄ alkyl substituted with 0-3 R^{5b};
C₂-C₄ alkenyl substituted with 0-3 R^{5b};
C₂-C₄ alkynyl substituted with 0-3 R^{5b};

R^{5a} is H, methyl, ethyl, propyl, or butyl;

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, Cl, F, Br, I, =O;
C₃-C₆ carbocycle substituted with 0-3 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
3 R^{5c};

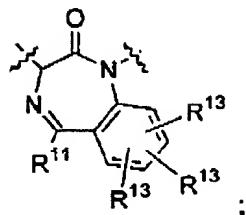
R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,
NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy,
C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁶ is H;

R⁷, at each occurrence, is independently selected from H, F, CF₃, methyl, and ethyl;

Ring B is

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 83 of 89**R11** is selected from

- H, C₁-C₄ alkoxy, Cl, F, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷, CF₃;
- C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};
- C₆-C₁₀ aryl substituted with 0-3 R^{11b};
- C₃-C₆ carbocycle substituted with 0-3 R^{11b}; or
- 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b};

R11a, at each occurrence, is independently selected from H, C₁-C₄ alkyl, OR¹⁴, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};**R11b**, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;**Z** is C₁-C₄ alkyl substituted with 1-3 R¹²;

- C₂-C₄ alkenyl substituted with 1-3 R¹²;
- C₂-C₄ alkynyl substituted with 1-3 R¹²;
- C₆-C₁₀ aryl substituted with 0-4 R^{12b};
- C₃-C₆ carbocycle substituted with 0-4 R^{12b}; or
- 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b};

R12, at each occurrence, is independently selected from

- C₆-C₁₀ aryl substituted with 0-4 R^{12b};
- C₃-C₆ carbocycle substituted with 0-4 R^{12b}; or

CT01/HOFF/HA/216624.1

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

*Response to Final Office Action
Mailed 04/08/2005
Page 84 of 89*

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₄ alkyl, or C₂-C₄ alkoxyalkyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from H, OH, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl, phenyl substituted by 0-3 R^{17a}, or -CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

R¹⁸, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from H, methyl, and ethyl;

provided, when R¹³ is H,

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 85 of 89

then Z is butyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²; or
C₂-C₄ alkynyl substituted with 1-3 R¹².

63. (PREVIOUSLY PRESENTED) A pharmaceutical composition comprising a compound according to Claim 57 and a pharmaceutically acceptable carrier.

64. (PREVIOUSLY PRESENTED) A pharmaceutical composition comprising a compound according to Claim 58 and a pharmaceutically acceptable carrier.

65. (PREVIOUSLY PRESENTED) A pharmaceutical composition comprising a compound according to Claim 59 and a pharmaceutically acceptable carrier.

66. (PREVIOUSLY PRESENTED) A pharmaceutical composition comprising a compound according to Claim 60 and a pharmaceutically acceptable carrier.

67. (PREVIOUSLY PRESENTED) A pharmaceutical composition comprising a compound according to Claim 61 and a pharmaceutically acceptable carrier.

68.(PREVIOUSLY PRESENTED) A pharmaceutical composition comprising a compound according to Claim 62 and a pharmaceutically acceptable carrier.

69.(PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 57.

U.S. Appl. No. 09/505,788; filed Feb 17, 2005

Response to Final Office Action
Mailed 04/08/2005
Page 86 of 89

70.(PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 58.

71. (PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 59.

72. (PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 60.

73. (PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 61.

74.(PREVIOUSLY PRESENTED) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 62.